

Application No. 09/843,167

Amendment dated September 3, 2003

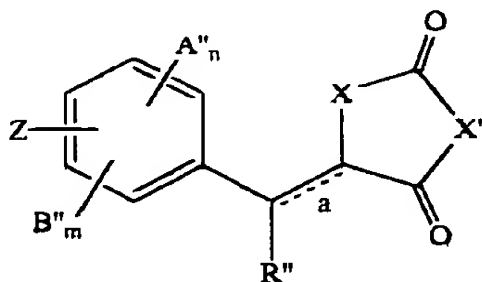
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Amendments to the Claims:

The following claims will replace all prior versions of the claims in this application (in the unlikely event that no claims follow herein, the previously pending claims will remain):

1-60. (Cancelled)

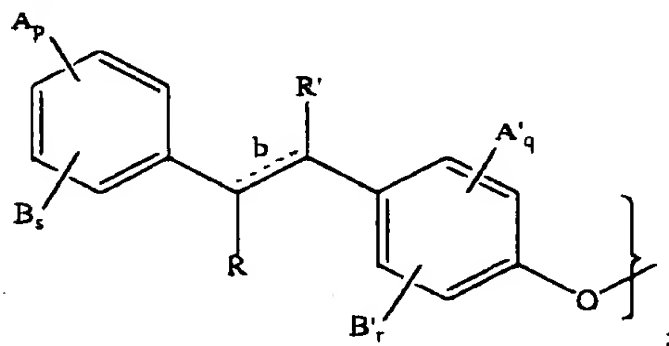
61. (New) A method of treating diabetes comprising the steps of administering to a subject suffering from a diabetic condition, a therapeutically effective amount of a compound represented by the following formula 1:



[1]

in a physiologically acceptable carrier;

wherein Z is



n, m, q and r independently represent integers from zero to 4 provided that $n + m \leq 4$ and $q + r \leq 4$; p and s independently represent integers from zero to 5 provided that $p + s \leq 5$; a and b represent double bonds which may be present or absent; when present, the double bonds may

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be in the E or Z configuration and, when absent, the resulting stereocenters may have the R- or S- configuration;

R and R' each independently represent a hydrogen atom; linear or branched C₁-C₂₀ alkyl; linear or branched C₂-C₂₀ alkenyl; -CO₂Z'; -CO₂R'''; -NH₂; -NHR'''; -NR₂'''; -OH; -OR'''; -CONR₂''''; halogen atom; optionally substituted linear or branched C₁-C₂₀ alkyl; optionally substituted linear or branched C₂-C₂₀ alkenyl;

R'' independently represents a hydrogen atom; linear or branched C₁-C₂₀ alkyl; linear or branched C₂-C₂₀ alkenyl; -CO₂Z'; -CO₂R'''; -NH₂; -NHR'''; -NR₂'''; -OH; -OR'''; halogen atom; optionally substituted linear or branched C₁-C₂₀ alkyl; optionally substituted linear or branched C₂-C₂₀ alkenyl;

R''' independently represents a linear or branched C₁-C₂₀ alkyl; linear or branched C₂-C₂₀ alkenyl; or -(CH₂)_x-Ar, where x represents an integer from 1 to 6 and Ar represents aryl;

R'''' independently represents a hydrogen atom; optionally substituted C₁-C₂₀ alkyl; optionally substituted C₁-C₂₀ alkoxy; optionally substituted C₂-C₂₀ alkenyl; optionally substituted C₆-C₁₀ aryl; or NR₂'''' represents a cyclic moiety.

Z' represents a hydrogen atom or a pharmaceutically acceptable counter-ion;

A, A' and A'' each independently represent a hydrogen atom; C₁-C₂₀ acylamino; C₁-C₂₀ acyloxy; C₁-C₂₀ alkanoyl; C₁-C₂₀ alkoxycarbonyl; C₁-C₂₀ alkoxy; C₁-C₂₀ alkylamino; C₁-C₂₀ alkylcarboxylamino; carboxyl; cyano; halo; or hydroxy;

B, B' and B'' each independently represent; C₂-C₂₀ alkenoyl; aroyl; aralkanoyl; nitro, optionally substituted, linear or branched C₁-C₂₀ alkyl; or optionally substituted, linear or branched C₂-C₂₀ alkenyl;

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or A and B jointly, A' and B' jointly, or A" and B" jointly, independently represent a methylenedioxy or ethylenedioxy group; and

X and X' independently represent >NH, >NR''', -O-, or -S-.

C1 62. (New) A method according to claim 61, wherein R' represents -CO₂R'''; or -CONR₂''' wherein R''' represents hydrogen or methyl or at least one R''' independently represents a hydrogen atom, methyl, or methoxy.

63. (New) A method according to claim 61, wherein R' represents -CO₂R''' wherein R''' represents hydrogen or methyl.

64. (New) A method according to claim 61, wherein R' represents -CONR₂''' wherein both R''' are the same and represent a hydrogen atom, methyl, or methoxy.

B1
contd 65. (New) A method according to claim 61, wherein X is -S- and X' is >NH.

66. (New) A method according to claim 62, wherein X is -S- and X' is >NH.

67. (New) A method according to claim 63, wherein X is -S- and X' is >NH.

68. (New) A method according to claim 64, wherein X is -S- and X' is >NH.

C2 69. (New) A method according to claim 62, wherein a represents a single bond and b represents a double bond.

70. (New) A method according to claim 62, wherein at least two A groups represent methoxy.

71. (New) A method according to claim 62, wherein at least two A groups represent a hydrogen bond.

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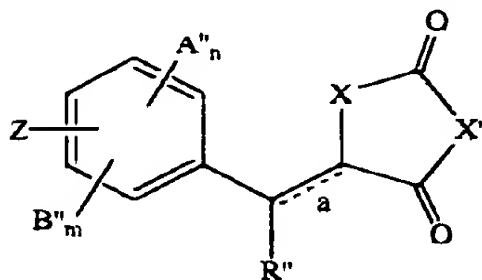
72. (New) A method according to claim 70, wherein at least two A groups represent a hydrogen bond.

73. (New) A method according to claim 61, wherein R' is carbomethoxy and A is methoxy.

74. (New) The method of claim 61 wherein said pharmaceutically acceptable counter ion is selected from sodium, potassium, calcium, magnesium, ammonium, tromethamine, or tetramethylammonium.

75. (New) The method of claim 62 wherein said pharmaceutically acceptable counter ion is selected from sodium, potassium, calcium, magnesium, ammonium, tromethamine, or tetramethylammonium.

76. (New). A method of treating diabetes comprising the steps of administering to a subject suffering from a diabetic condition, a therapeutically effective amount of a compound represented by the following formula 1:



[1]

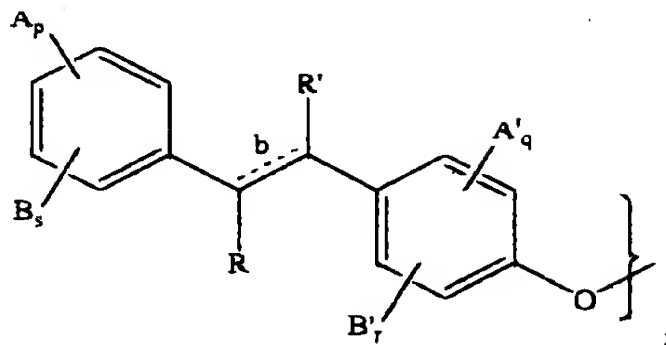
in a physiologically acceptable carrier;

wherein Z is

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H; A''; or B'';

n , m , q and r independently represent integers from zero to 4 provided that $n + m \leq 4$ and $q + r \leq 4$; p and s independently represent integers from zero to 5 provided that $p + s \leq 5$; a and b represent double bonds which may be present or absent; when present, the double bonds may be in the E or Z configuration and, when absent, the resulting stereocenters may have the R- or S- configuration;

R and R' each independently represent a hydrogen atom; linear or branched C₁-C₂₀ alkyl; linear or branched C₂-C₂₀ alkenyl; -CO₂Z'; -CO₂R'''; -NH₂; -NHR'''; -NR₂'''; -OH; -OR'''; -CONR₂''''; halogen atom; optionally substituted linear or branched C₁-C₂₀ alkyl; optionally substituted linear or branched C₂-C₂₀ alkenyl;

R'' independently represents a hydrogen atom; linear or branched C₁-C₂₀ alkyl; linear or branched C₂-C₂₀ alkenyl; -CO₂Z'; -CO₂R'''; -NH₂; -NHR'''; -NR₂'''; -OH; -OR'''; halogen atom; optionally substituted linear or branched C₁-C₂₀ alkyl; optionally substituted linear or branched C₂-C₂₀ alkenyl;

R''' independently represents a linear or branched C₁-C₂₀ alkyl; linear or branched C₂-C₂₀ alkenyl; or -(CH₂)_x-Ar, where x represents an integer from 1 to 6 and Ar represents aryl;

R'''' independently represents a hydrogen atom; optionally substituted C₁-C₂₀ alkyl; optionally substituted C₁-C₂₀ alkoxy; optionally substituted C₂-C₂₀ alkenyl; optionally substituted C₆-C₁₀ aryl; or NR₂'''' represents a cyclic moiety.

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Z' represents a hydrogen atom or a pharmaceutically acceptable counter-ion;

A, and A' each independently represent a hydrogen atom; C₁-C₂₀ acylamino; C₁-C₂₀ acyloxy; C₁-C₂₀ alkanoyl; C₁-C₂₀ alkoxycarbonyl; C₁-C₂₀ alkoxy; C₁-C₂₀ alkylamino; C₁-C₂₀ alkylcarboxylamino; carboxyl; cyano; halo; or hydroxy;

A'' independently represent a hydrogen atom; C₁-C₂₀ acylamino; C₁-C₂₀ acyloxy; C₁-C₂₀ alkanoyl; C₁-C₂₀ alkoxycarbonyl; C₁-C₂₀ alkylamino; C₁-C₂₀ alkylcarboxylamino; carboxyl; cyano; or halo;

B, B' and B'' each independently represent; C₂-C₂₀ alkenoyl; aroyl; aralkanoyl; nitro; optionally substituted, linear or branched C₁-C₂₀ alkyl; or optionally substituted, linear or branched C₂-C₂₀ alkenyl;

or A and B jointly, A' and B' jointly, or A'' and B'' jointly, independently represent a methylenedioxy or ethylenedioxy group; and

X and X' independently represent >NH, >NR'', -O-, or -S-.

77. (New) A method according to claim 76, wherein R' represents -CO₂R''; or -CONR₂''' wherein R''' represents hydrogen or methyl or at least one R'''' independently represents a hydrogen atom, methyl, or methoxy.

78. (New) A method according to claim 76, wherein R' represents -CO₂R''' wherein R''' represents hydrogen or methyl.

79. (New) A method according to claim 76, wherein R' represents -CONR₂''' wherein both R'''' are the same and represent a hydrogen atom, methyl, or methoxy.

80. (New) A method according to claim 76, wherein X is -S- and X' is >NH.

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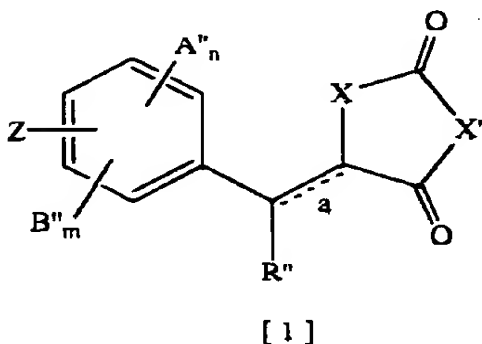
81. (New) A method according to claim 77, wherein X is -S- and X' is >NH.
82. (New) A method according to claim 78, wherein X is -S- and X' is >NH.
83. (New) A method according to claim 79, wherein X is -S- and X' is >NH.
84. (New) A method according to claim 77, wherein a represents a single bond and b represents a double bond.
85. (New) A method according to claim 77, wherein at least two A groups represent methoxy.
86. (New) A method according to claim 77, wherein at least two A groups represent a hydrogen bond.
87. (New) A method according to claim 85, wherein at least two A groups represent a hydrogen bond.
88. (New) A method according to claim 76, wherein R' is carbomethoxy and A is methoxy.
89. (New) The method of claim 76 wherein said pharmaceutically acceptable counter ion is selected from sodium, potassium, calcium, magnesium, ammonium, tromethamine, or tetramethylammonium.
90. (New) The method of claim 77 wherein said pharmaceutically acceptable counter ion is selected from sodium, potassium, calcium, magnesium, ammonium, tromethamine, or tetramethylammonium.

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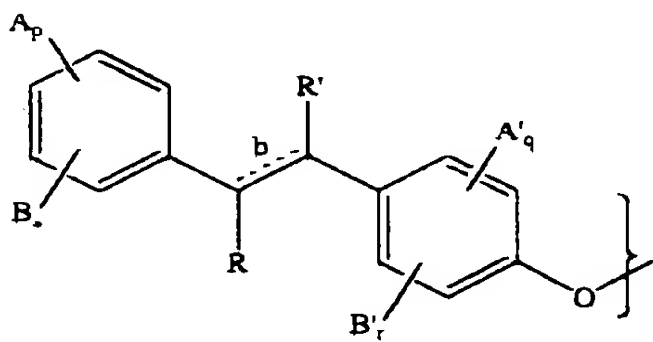
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91. (New) A method of treating diabetes comprising the steps of administering to a subject suffering from a diabetic condition, a therapeutically effective amount of a compound represented by the following formula 1:

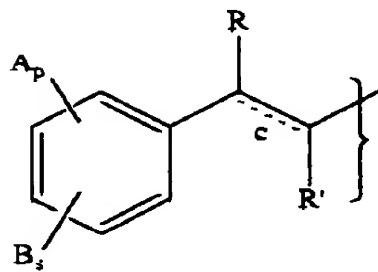


in a physiologically acceptable carrier;

wherein Z is



or



B contd

n, m, q and r independently represent integers from zero to 4 provided that $n + m \leq 4$ and $q + r \leq 4$; p and s independently represent integers from zero to 5 provided that $p + s \leq 5$; a, b and c represent double bonds which may be present or absent; when present, the double bonds

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may be in the E or Z configuration and, when absent, the resulting stereocenters may have the R- or S- configuration;

R independently represents a hydrogen atom; linear or branched C₁-C₂₀ alkyl; linear or branched C₂-C₂₀ alkenyl; -CO₂Z'; -CO₂R'''; -NH₂; -NHR'''; -NR₂'''; -OH; -OR'''; -CONR₂'''; halogen atom; optionally substituted linear or branched C₁-C₂₀ alkyl; optionally substituted linear or branched C₂-C₂₀ alkenyl;

R' independently represents a hydrogen atom; linear or branched C₁-C₂₀ alkyl; linear or branched C₂-C₂₀ alkenyl; -CO₂Z'; -CO₂R'''; -NH₂; -NHR'''; -NR₂'''; -OR'''; -CONR₂'''; halogen atom; optionally substituted linear or branched C₁-C₂₀ alkyl; optionally substituted linear or branched C₂-C₂₀ alkenyl;

R'' independently represents a hydrogen atom; linear or branched C₁-C₂₀ alkyl; linear or branched C₂-C₂₀ alkenyl; -CO₂Z'; -CO₂R'''; -NH₂; -NHR'''; -NR₂'''; -OH; -OR'''; halogen atom; optionally substituted linear or branched C₁-C₂₀ alkyl; optionally substituted linear or branched C₂-C₂₀ alkenyl;

R''' independently represents a linear or branched C₁-C₂₀ alkyl; linear or branched C₂-C₂₀ alkenyl; or -(CH₂)_x-Ar, where x represents an integer from 1 to 6 and Ar represents aryl;

R'''' independently represents a hydrogen atom; optionally substituted C₁-C₂₀ alkyl; optionally substituted C₁-C₂₀ alkoxy; optionally substituted C₂-C₂₀ alkenyl; optionally substituted C₆-C₁₀ aryl; or NR₂'''' represents a cyclic moiety.

Z' represents a hydrogen atom or a pharmaceutically acceptable counter-ion;

A, A' and A'' each independently represent a hydrogen atom; C₁-C₂₀ acylamino; C₁-C₂₀ acyloxy; C₁-C₂₀ alkanoyl; C₁-C₂₀ alkoxy; C₁-C₂₀ alkoxycarbonyl; C₁-C₂₀ alkylamino; C₁-C₂₀ alkylcarboxylamino; carboxyl; cyano; halo; or hydroxy;

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B, B' and B'' each independently represent; C₂-C₂₀ alkenoyl; aroyl; aralkanoyl; nitro; optionally substituted, linear or branched C₁-C₂₀ alkyl; or optionally substituted, linear or branched C₂-C₂₀ alkenyl;

or A and B jointly, A' and B' jointly, or A'' and B'' jointly, independently represent a methylenedioxy or ethylenedioxy group; and

X and X' independently represent >NH, >NR''', -O-, or -S-.

92. (New) A method according to claim 91, wherein R' represents -CO₂R'''; or -CONR₂''' wherein R''' represents hydrogen or methyl or at least one R''' independently represents a hydrogen atom, methyl, or methoxy.

93. (New) A method according to claim 91, wherein R' represents -CO₂R''' wherein R''' represents hydrogen or methyl.

94. (New) A method according to claim 91, wherein R' represents -CONR₂''' wherein both R''' are the same and represent a hydrogen atom, methyl, or methoxy.

95. (New) A method according to claim 91, wherein X is -S- and X' is >NH.

96. (New) A method according to claim 92, wherein X is -S- and X' is >NH.

97. (New) A method according to claim 93, wherein X is -S- and X' is >NH.

98. (New) A method according to claim 94, wherein X is -S- and X' is >NH.

99. (New) A method according to claim 92, wherein a represents a single bond and b represents a double bond.

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100. (New) A method according to claim 92, wherein at least two A groups represent methoxy.

101. (New) A method according to claim 92, wherein at least two A groups represent a hydrogen bond.

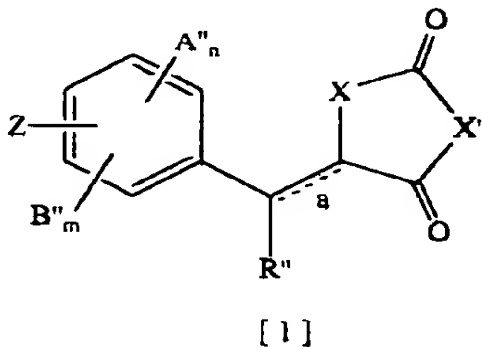
102. (New) A method according to claim 100, wherein at least two A groups represent a hydrogen bond.

103. (New) A method according to claim 91, wherein R' is carbomethoxy and A is methoxy.

c1 104. (New) The method of claim 91 wherein said pharmaceutically acceptable counter ion is selected from sodium, potassium, calcium, magnesium, ammonium, tromethamine, or tetramethylammonium.

105. (New) The method of claim 92 wherein said pharmaceutically acceptable counter ion is selected from sodium, potassium, calcium, magnesium, ammonium, tromethamine, or tetramethylammonium.

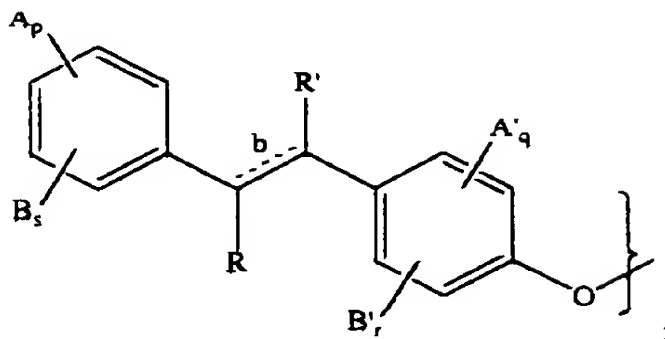
106. (New) A method of treating diabetes comprising the steps of administering to a subject suffering from a diabetic condition, a therapeutically effective amount of a compound represented by the following formula 1:



in a physiologically acceptable carrier;

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wherein Z is



n, m, q and r independently represent integers from zero to 4 provided that $n + m \leq 4$ and $q + r \leq 4$; p and s independently represent integers from zero to 5 provided that $p + s \leq 5$; a and b represent double bonds which may be present or absent; when present, the double bonds may be in the E or Z configuration and, when absent, the resulting stereocenters may have the R- or S- configuration;

R and R' each independently represent a hydrogen atom; linear or branched C_1 - C_{20} alkyl; linear or branched C_2 - C_{20} alkenyl; $-CO_2Z'$; $-CO_2R'''$; $-NH_2$; $-NHR'''$; $-NR_2'''$; $-OH$; $-OR'''$; halogen atom; optionally substituted linear or branched C_1 - C_{20} alkyl; optionally substituted linear or branched C_2 - C_{20} alkenyl;

R'' independently represents a hydrogen atom; linear or branched C_1 - C_{20} alkyl; linear or branched C_2 - C_{20} alkenyl; $-CO_2Z'$; $-CO_2R'''$; $-NH_2$; $-NHR'''$; $-NR_2'''$; $-OH$; $-OR'''$; halogen atom; optionally substituted linear or branched C_1 - C_{20} alkyl; optionally substituted linear or branched C_2 - C_{20} alkenyl;

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R''' independently represents a linear or branched C₁-C₂₀ alkyl; linear or branched C₂-C₂₀ alkenyl; or -(CH₂)_x-Ar, where x represents an integer from 1 to 6 and Ar represents aryl;

Z' represents a hydrogen atom or a pharmaceutically acceptable counter-ion;

A, A' and A'' each independently represent a hydrogen atom; C₁-C₂₀ acylamino; C₁-C₂₀ acyloxy; C₁-C₂₀ alkanoyl; C₁-C₂₀ alkoxy; C₁-C₂₀ alkoxy; C₁-C₂₀ alkylamino; C₁-C₂₀ alkylcarboxylamino; carboxyl; cyano; halo; or hydroxy;

B, B' and B'' each independently represent; C₂-C₂₀ alkenoyl; aroyl; aralkanoyl; nitro; optionally substituted, linear or branched C₁-C₂₀ alkyl; or optionally substituted, linear or branched C₂-C₂₀ alkenyl;

or A and B jointly, A' and B' jointly, or A'' and B'' jointly, independently represent a methylenedioxy or ethylenedioxy group; and

X and X' independently represent >NH, >NR''', -O-, or -S-.

107. (New) A method according to claim 106, wherein R' represents -CO₂R''' wherein R''' represents hydrogen or methyl.

108. (New) A method according to claim 106, wherein X is -S- and X' is >NH.

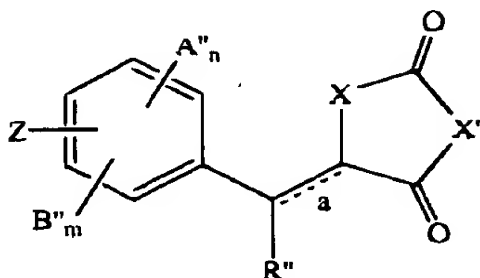
109. (New) A method according to claim 107, wherein X is -S- and X' is >NH.

110. (New). A method of treating diabetes comprising the steps of administering to a subject suffering from a diabetic condition, a therapeutically effective amount of a compound represented by the following formula 1:

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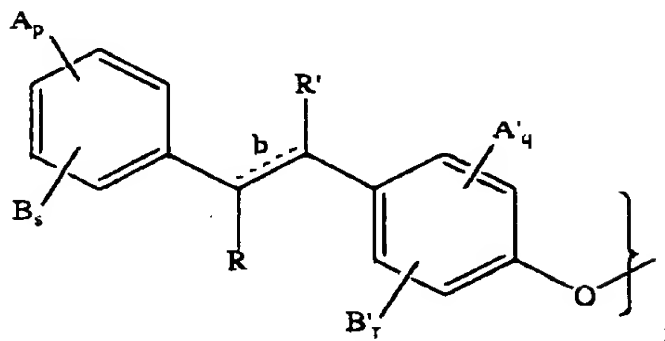
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[1]

in a physiologically acceptable carrier;

wherein Z is



H; A''; or B'';

B1 cont'd

n, m, q and r independently represent integers from zero to 4 provided that $n + m \leq 4$ and $q + r \leq 4$; p and s independently represent integers from zero to 5 provided that $p + s \leq 5$; a and b represent double bonds which may be present or absent; when present, the double bonds may be in the E or Z configuration and, when absent, the resulting stereocenters may have the R- or S- configuration;

R and R' each independently represent a hydrogen atom; linear or branched C_1 - C_{20} alkyl; linear or branched C_2 - C_{20} alkenyl; $-CO_2Z'$; $-CO_2R'''$; $-NH_2$; $-NHR'''$; $-NR_2'''$; $-OH$; $-OR'''$;

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halogen atom; optionally substituted linear or branched C₁-C₂₀ alkyl; optionally substituted linear or branched C₂-C₂₀ alkenyl;

R'' independently represents a hydrogen atom; linear or branched C₁-C₂₀ alkyl; linear or branched C₂-C₂₀ alkenyl; -CO₂Z'; -CO₂R'''; -NH₂; -NHR'''; -NR₂'''; -OH; -OR'''; halogen atom; optionally substituted linear or branched C₁-C₂₀ alkyl; optionally substituted linear or branched C₂-C₂₀ alkenyl;

R''' independently represents a linear or branched C₁-C₂₀ alkyl; linear or branched C₂-C₂₀ alkenyl; or -(CH₂)_x-Ar, where x represents an integer from 1 to 6 and Ar represents aryl;

Z' represents a hydrogen atom or a pharmaceutically acceptable counter-ion;

A, and A' each independently represent a hydrogen atom; C₁-C₂₀ acylamino; C₁-C₂₀ acyloxy; C₁-C₂₀ alkanoyl; C₁-C₂₀ alkoxycarbonyl; C₁-C₂₀ alkoxy; C₁-C₂₀ alkylamino; C₁-C₂₀ alkylcarboxylamino; carboxyl; cyano; halo; or hydroxy;

A'' independently represent a hydrogen atom; C₁-C₂₀ acylamino; C₁-C₂₀ acyloxy; C₁-C₂₀ alkanoyl; C₁-C₂₀ alkoxycarbonyl; C₁-C₂₀ alkylamino; C₁-C₂₀ alkylcarboxylamino; carboxyl; cyano; or halo;

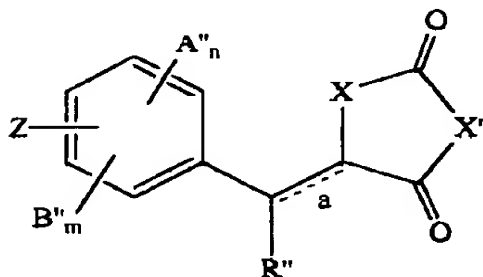
B, B' and B'' each independently represent; C₂-C₂₀ alkenoyl; aroyl; aralkanoyl; nitro; optionally substituted, linear or branched C₁-C₂₀ alkyl; or optionally substituted, linear or branched C₂-C₂₀ alkenyl;

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or A and B jointly, A' and B' jointly, or A'' and B'' jointly, independently represent a methylenedioxy or ethylenedioxy group; and

X and X' independently represent >NH, >NR'', -O-, or -S-.

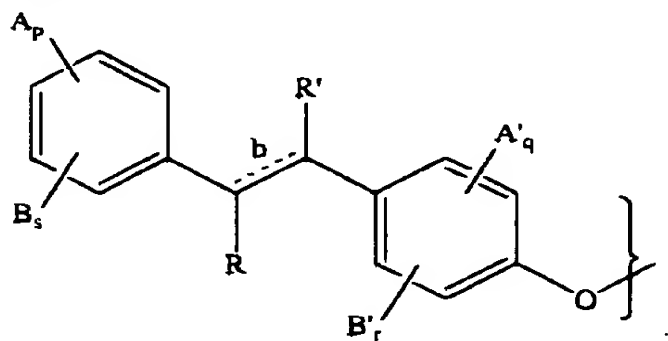
111. (New) A method of treating diabetes comprising the steps of administering to a subject suffering from a diabetic condition, a therapeutically effective amount of a compound represented by the following formula 1:



[1]

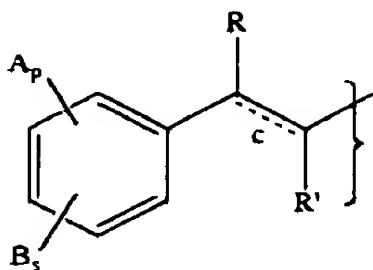
in a physiologically acceptable carrier;

wherein Z is



or

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n , m , q and r independently represent integers from zero to 4 provided that $n + m \leq 4$ and $q + r \leq 4$; p and s independently represent integers from zero to 5 provided that $p + s \leq 5$. a , b and c represent double bonds which may be present or absent; when present, the double bonds may be in the E or Z configuration and, when absent, the resulting stereocenters may have the R- or S- configuration;

R independently represents a hydrogen atom; linear or branched C_1 - C_{20} alkyl; linear or branched C_2 - C_{20} alkenyl; $-\text{CO}_2\text{Z}'$; $-\text{CO}_2\text{R}'''$; $-\text{NH}_2$; $-\text{NHR}'''$; $-\text{NR}_2'''$; $-\text{OH}$; $-\text{OR}'''$; halogen atom; optionally substituted linear or branched C_1 - C_{20} alkyl; optionally substituted linear or branched C_2 - C_{20} alkenyl;

R' independently represents a hydrogen atom; linear or branched C_1 - C_{20} alkyl; linear or branched C_2 - C_{20} alkenyl; $-\text{CO}_2\text{Z}'$; $-\text{CO}_2\text{R}'''$; $-\text{NH}_2$; $-\text{NHR}'''$; $-\text{NR}_2'''$; $-\text{OR}'''$; $-\text{CONR}_2'''$; halogen atom; optionally substituted linear or branched C_1 - C_{20} alkyl; optionally substituted linear or branched C_2 - C_{20} alkenyl;

R'' independently represents a hydrogen atom; linear or branched C_1 - C_{20} alkyl; linear or branched C_2 - C_{20} alkenyl; $-\text{CO}_2\text{Z}'$; $-\text{CO}_2\text{R}'''$; $-\text{NH}_2$; $-\text{NHR}'''$; $-\text{NR}_2'''$; $-\text{OH}$; $-\text{OR}'''$; halogen atom; optionally substituted linear or branched C_1 - C_{20} alkyl; optionally substituted linear or branched C_2 - C_{20} alkenyl;

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R''' independently represents a linear or branched C₁-C₂₀ alkyl; linear or branched C₁-C₂₀ alkenyl; or -(CH₂)_x-Ar, where x represents an integer from 1 to 6 and Ar represents aryl;

Z' represents a hydrogen atom or a pharmaceutically acceptable counter-ion;

A, A' and A'' each independently represent a hydrogen atom; C₁-C₂₀ acylamino; C₁-C₂₀ acyloxy; C₁-C₂₀ alkanoyl; C₁-C₂₀ alkoxy; C₁-C₂₀ alkylamino; C₁-C₂₀ alkylcarboxylamino; carboxyl; cyano; halo; or hydroxy;

B, B' and B'' each independently represent: C₂-C₂₀ alkenoyl; aroyl; aralkanoyl; nitro; optionally substituted, linear or branched C₁-C₂₀ alkyl; or optionally substituted, linear or branched C₂-C₂₀ alkenyl;

or A and B jointly, A' and B' jointly, or A'' and B'' jointly, independently represent a methylenedioxy or ethylenedioxy group; and

X and X' independently represent >NH, >NR''', -O-, or -S-.

112. (New) A method of treating diabetes comprising the steps of administering to a subject suffering from a diabetic condition, a therapeutically effective amount of 3-(3,5-dimethoxyphenyl)-2-[4-[4-(2,4-dioxothiazolidin-5-ylmethyl)-phenoxy]-phenyl]-acrylic acid in a physiologically acceptable carrier.

113. (New) A method of treating diabetes comprising the steps of administering to a subject suffering from a diabetic condition, a therapeutically effective amount of 3-(3,5-dimethoxyphenyl)-2-[4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl]-acrylamide in a physiologically acceptable carrier.

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cont'd

114. (New) A method of treating diabetes comprising the steps of administering to a subject suffering from a diabetic condition, a therapeutically effective amount of 5-(4-(4-(1-carbomethoxy-2-(3,5-dimethoxy phenyl) ethenyl)-phenoxy)-benzyl)-2,4-thiazolidinedione in a physiologically acceptable carrier.
